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39

CRITICAL ANALYSIS, ERRONEOUS INFORMATION, MISSING DATA AND EDITORIAL STATEMENTS IN THE SCIENTIFIC LITERATURE, REVIEW OF GLUTAMATE BY TRACOR JITCO CO.

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Volume 4-Critical Analysis, Erroneous Information, Missing Data & Editorial Statements in the Scientific literature, Review of Glutamate by Tracor Jitco, Company-IGTC-5/74

INTERNATIONAL GLUTAMATE TECHNICAL COMMITTEE

EUROPE – Dr. T. A. Giacometti
JAPAN – Dr. T. Tsunoda
TAIWAN – Dr. T. C. Tung
U.S.A. – Dr. A. Ebert

PLEASE REPLY TO:

85 Walnut Street
Watertown, Mass. 02172

CRITICAL ANALYSIS
SUMMARY OF ERRONEOUS INFORMATION
MISSING DATA AND
EDITORIAL STATEMENTS IN
THE SCIENTIFIC LITERATURE REVIEW
OF GLUTAMATE BY TRACOR JITCO CO.

Critical Analysis

ANALYSIS OF TRACOR - JITCO SLR ON GLUTAMATES

Introduction -

Regretably, this detailed review from a comprehensive bibliography (8365 references) largely misses the point of the entire goal behind gathering data for the GRAS list review, namely examining studies designed to evaluate the safety of food additives according to patterns of their use in food. Thus, such a scientific literature review should be organized to evaluate in detail those studies where the test compound was administered in amounts, concentrations, routes and preferably in formulations, common to its use by man.

Toxicological Evaluation of Foods and Food Components -

The heart of the toxicological evaluation of any food, food component or food additive is a series of acute, subacute and chronic studies in which the test compound is fed - or certainly given by other oral means -at levels equivalent to its exposure to man and reasonable multiples thereof. The subacute and chronic feeding studies completed on various glutamates are conspicuous by their absence from the scientific literature review on glutamate. Furthermore, in those studies where glutamate was fed, the reviewer makes little or no mention of the data (even if such data were collected as a supplement to the stated goal of a given experiment) where administration of glutamate equivalent to its use by man was without toxic effect.

Induction of Toxic Manifestations -

There is no doubt that test systems are available in which marked effects from massive doses of glutamate may be observed. However, the authors in presenting a wordy review and creating a voluminous report neglect to:

A. Differentiate sensitive species from non-sensitive ones in terms of glutamate effect.

B. Point out that confirmed glutamate effects are confined to mice, whereas higher (phylogenetic) species, namely dogs, cats, guinea pigs, pigs and primates (including man), show no evidence of the marked toxicologic effects induced in the mouse- and then usually from massive doses by glutamate - given parenterally.

C. Relate doses, routes of administration and concentrations of test materials used in studies to induce toxicity with those used by man and with that research where glutamate was without effect. Such would have indicated that it would be approaching the impossible to physically get such massive amounts and concentrations into man.

By structuring the Scientific Literature Review to report studies on toxic manifestations, data from reserach where no effects were seen, were almost by definition, ignored by the reviewer. By failing to state

the relevant feeding studies, the impression is created that the literature consists essentially of data suggesting that this amino acid is unsafe to man, when, in fact, what the data really indicates is that: the current food use patterns of glutamate are safe to man and, that under a variety of abusive conditions, several toxic manifestations can be demonstrated from glutamate as well as a variety of other food constituents (largely ignored in this review). Careful perusal of the missing data and papers on glutamate feeding clearly indicate that the summary inaccurately and incompletely reflects the data available, and in a highly opinionated fashion.

Erroneous Consumption Data -

In addition, through no fault of the contractor, the review lists use pattern data and total production figures for salts of glutamic acid as gleaned from the NAS/NRC survey which are totally erroneous; in some cases 400% higher than known usage of glutamates. The review, in effect creates "average data" numbers which in no way agree with known production data. We note as well, per capita consumption figures which are clearly not reflective of use patterns of glutamate salts.

Further, the voluminous bibliography attached to the review illustrates that extensive publications have appeared in the scientific literature over the years, but the consideration of data in writing the summary essentially ends with papers published approximately three years ago. Thus, a number

of pertinent papers which well illuminate the conditions needed to induce glutamate toxicity - hence the conditions for its current safe use by man are not discussed in the review.

Erroneous Infor.

I. Errors in Fact - Summary

P	¶	ℓ	Error Stated	Comment
Numerous			Structural formulas referred to in Text - incorrect formulae for salts are listed. Also lists antiquated non used synonyms e.g. Glutamatic Acid, Glutaminic Acid.	See Food Technology Texts or Reference Books e.g. Food Chemicals Codex for correct formulae.
i	3	2	MPG Listed as Hygroscopic	MPG Hygroscopicity not a portion of U.S. standards
i	4	2	MSG listed as non hygroscopic	Do not believe either salt, MSG or MPG is either hygroscopic or non-hygroscopic.
i	5	1	GA·HCl formula listed As $C_5H_8NO_4 \cdot HCl$	Correct Formula is $C_5H_9NO_4 \cdot HCl$
ii	2	3	LD_{50} for MSG Listed as 1920mg/kg Mouse 1660mg/kg Rat	Correct data are 10 fold higher 19.20(22.84-16.13)g/kg Mice 16.60(18.90-14.50)g/kg Rats
iv	3	4	Myers sp	Mayer
v	2	3	Authors "commented that on close scrutiny the only data that appeared to conflict with Olneys were those of Adamo & Ratner.	This paper does not state this conclusion
vii	3	1	Randolph & Williams. MSG derived from beets by fermentation.	In Randolph & Rollins paper product was derived by extraction, not fermentation.

P	¶	ℓ	Error Stated	Comment
xi	3	3	The rabbits were fed 25 g/kg daily for 40 days	The rabbits were fed 25mg/kg of glutamic acid hydrochloride daily as "Glutamidine", a pharmaceutical based on glutamic acid hydrochloride, for 1 month.
xiii	2	7	(4211) Ref.	(2411)

Comment

P	¶	ℓ	
xv	3	1	States that NAS-Survey reported 75,000 tons of MSG representing 60-70% of the poundage actually added to the nations food supply -were produced by the firms it surveyed. 75,000 tons @ 60-70% = 125,000 tons of glutamate used. Actual U.S. production for 1971 = 23,400 tons and approximately 5,000 tons imported thus the data reported are 400+% too high. For production data and import data see data produced by U.S. Tariff Commission Report (Flavor and Perfume Materials) and Journal of Commerce import/export data.
xv	3	1	Averaging usage levels ranged from 0.15% to 0.24% Usage levels are higher up to 1.00% in certain products.
xv	3	1	NAS/NRC Survey...reported that "75,000 tons (representing 60-70% of the poundage actually added to the nation's food supply) were produced.." Total US production is, in fact not over 25,000 tons with not over 5,000 tons imported - Thus at least a 400% error on total usage is listed.
xvi	2	1	Lists intakes as MAG 5267.5 mg and 1160 mg for MSG. All current production data indicate that sodium salt usage far exceeds that of the ammonium salt.

P	¶	ℓ	Error Stated	Comment
xvi	1	12	The FAO/WHO Committee noted that infants & children were often fed MSG - containing foods intended for adults, and that consequences might not appear until later in the childs development.	The FAO/WHO report makes no such statement, it reads in part: "...In view of the uncertainty regarding the possible susceptibility of the very early human neonate to high oral intakes of glutamate, it would be prudent not to add monosodium glutamate to foods specifically intended for infants under one year of age. When the further work on this aspect has become available, it may be possible to arrive at an Acceptable Daily Intake for these infants as well. * This figure later reduced to three months of age. Seventeenth report Joint FAO/WHO Expert Committee on Food Additives (CAC/FAL 1-1973).
xvi	2	4	3871mg monopotassium glutamate*	3871mg monoammonium glutamate *
xvi	2	5	2290.8mg MAG*	493.2mg MSG*

*Error in NAS/NRC Consumption Report.

Errors in Fact - Text

P	¶	ℓ	Error Stated	Comment
8	III		$HOOCCH(NH_2)CH_2CH_2COOH \cdot K \cdot H_2O$	Correct formula is $HOOCCH(NH_2)CH_2CH_2COOK \cdot H_2O$
12	III		$HOOCCH(NH_2)CH_2CH_2COOH \cdot Na \cdot H_2O$	Correct formula is $HOOCCH(NH_2)CH_2CH_2COONa \cdot H_2O$
30	2	1	"Glutamic acid is stated to comprise about 20% of total amino acids found in natural protein sources".	In accuracy of statement implies some doubt - there is no doubt, the statement is factual.
30	2	2	Free glutamic acid occurs naturally in... the range levels of 0.005 - 0.23% (4862).	In fact it occurs at higher levels. See data for mushrooms P 34, cheese P 39, tomatoe P 34 of SLR.
30	3	all		The discussion of glutamate production is at least 30 years out of date and in no way informs the reader as to how glutamate is now produced on a worldwide basis.
46	1	1	4.4-4.5 mg/liter of free glutamic acid	Correct figures are 0.46 ± 0.16 mg/100ml.
46	1	1	0.9 mg/100ml of bound glutamic acid.	Correct figures are 10.8 ± 3.5 mg/100ml.
46	1	2	Human urine contains 2.1-3.9 µg/mg ·····	Correct figures are 2.9 ± 1.2 µg/mg of creatinine.
48	table			See comments on Summary for description of erroneous data.
48	Table 12 6-7		LD_{50} for Enzymatic casein hydrolysate	Should be removed because the data are not directly related to the safety evaluation of MSG.
49	Table 13		i.v.	i.p.
50	Table 14		MSG (mg/kg BW)	MSG (mg/g BW)

P	¶	ℓ	Error Stated	Comment
52	1	4	receiving 4-8 mg/g in single doses	receiving 2.20-5.40 mg/g in consecutive doses of 2-16 days.
58	1	5	in 5-day-old rats	in 5-, 10-, 12- and 20-day-old rats
58	1	6	strain not given	Rats of Sprague-Dawley strain were used.
58	1	15	(2) On the fifth postnatal day there was ·····, which declined on the tenth and again on the twelfth postnatal day.	This description is not always correct. "(2) On the fifth postnatal day there was a high uptake of isotopically labeled glutamate by brain and retina. On the tenth and the twelfth postnatal day difference in the levels of labeled glutamate with time in the brain and retina was observed with one another".
58	2	5	a 40% increase	a 30% increase
58	2	8	On the fifth postnatal day ····· on the twelfth postnatal day.	The words, "from plasma", should be removed because no description is found in the original report.
61	1	21	intraveneously (i.v.)	intraperitoneally (i.p.)
68	1	5	experimental females exceeding both experimental males and control females	experimental females gained more weight by comparison to controls of their own sex than did treated males
68	1	19	abnormally small	overall reduced in mass and in the number of cells
72	3	2	nuclei of day-old mice	nuclei of seven-day-old mice
72	3	2	Thirty-seven	Thirty mice
76	2	3	4 g/kg s.c. or by tube.	4 g/kg s.c.
76	3	5	habenar nuclei	habenular nuclei
76	4	1	Matsuyan	Matsuyama

P	¶	ℓ	Error Stated	Comment
77	2	1	Matsuyan	Matsuyama
78	2	1	MSA	MSG
84	1	2	MSG 4.4 g/kg	In the original paper, MSG 2.0 mmol/100g body weight was used. This dose is corresponding to MSG 3.4 g/kg.
86	1	1	MSG at 10% in diet, and also isocationic amounts of monopotassium glutamate (MKG), NaCl and KCl	Diets containing MSG and monopotassium glutamate (MKG), each 10%, or NaCl and KCl each equivalent to cation in the glutamate salt
88	1	2	DNA and protein analyses of homogenized whole brains.	RNA, DNA and protein analyses of homogenized whole brains and nucleus number and cellular size.
96	1	8	score	% score
96	1	12	67±17	-67±17
"	"	"	54±15	-54±15
114	2	2	24-147 g	25-147 g
118	3	1-2	light headedness or dizziness, and tightness of the face (18%)	light headedness (18%) and tightness in the face (12%)
138	3	1	Results of Aleksandrov et al.	Should be removed because DL-glutamic acid is not related to the safety evaluation of MSG.
138	4	1	three groups of rabbits 25mg/kg of glutamic acid for 40 days	Accurate statement is that three groups of rabbits 25 mg/kg of glutamic acid hydrochloride daily as "Glutamidine", a pharmaceutical based on glutamic acid hydrochloride, for one month.

P	¶	ℓ	Error Stated	Comment
139	4	2	found a higher incidence of ···· than in the experimental group	Important information of the experimental results is missing. Should be described as follows: "found no differences between the treated and control groups as to rate of conception, mean litter size and nursing rate. No external and skeletal malformations were observed in the young".
139	4	5	The authors noted that if MSG were ····· racemization to the D-form	Should be removed because no food is cooked or processed under the described condition.
140	3	1	"widespread clinical use of I.V. doses of glutamic acid"	I.V. clinical use of glutamic acid is extremely limited.
142	1	1	10% MSG, MKG, NaCl, or KCl	MSG and MKG each 10%, or NaCl and KCl each equivalent to the cation in the glutamate salt
156	4	1,3	Ref. 7787=Lancet, 2, 1(1949)	Ref. 7787=Lancet, 257, 1(1949)
156	4	4	····with 100g of food ····	····with 100g of food protein ·····
158	2	2	···· : the sodium or potassium salt, ·····	···· : the sodium salt, ····
160-163	4	1	According to Walshe (7840), ····· and cation transport in the brain and kidney (7840)	What is described in this paragraph should be refered to the reports of Quastel et al., Weil-Malherbe et al., Terner et al. and Stera et al. The description in this paper of Walshe is the effect of exogenous glutamate on the human coma subjects of hepatic failure.
163	2	2	···· penetration of ^{14}C-labeled glutaic acid····	···· penetration of U-^{14}C-labeled glutamic acid
168	2	2	···· diet of weanling rats.	···· diet of weanling male rats.

P	¶	ℓ	Error Stated	Comment
168	4	1	.... when glutamate was ...	.... when 2-^{14}C-DL-glutamic acid was ....
170	1	2	.... catabolism (see Fig.7)	This should be removed because Fig.7 does not relate to this paper directly.
174	2	1		The conclusion of the key point of this paper, the effects of dietary MSG on enzymes, is not clear. The following description, for example, should be added: no significant differences in GPT, GDH and GOT activities were noted by feeding of MSG.
182	3	1	.... ^{14}C-labeled L-glutamate	.... U-^{14}C-labeled L-glutamate
183	2	3	.... MSG	.... U-^{14}C-MSG
191	4	7	Serum cholesterol fell 31 mg	Serum cholesterol fell 37 mg .....
192	4	3	Cholesterol was 42±15.8 (SEM) mg/100ml	Cholesterol was 42±5.8 (SEM) mg/100ml
196	3	2	.... powdered seeweed used as a flavoring	In fact arid seeweed was used as a flavoring
202	3	6	MKG	MAG
202	3	7	2290.8	Correct figure is 493.2
213	3	5-6	However, intakes of 1500mg MSG have found to trigger allergic reactions in sensitive individuals	Accurate statement is that quantities less than 2 g/serving would have no more chance of producing symptoms than seasoned juice containing no added MSG.

PRODUCTION AND CONSUMPTION

Unfortunately there are several unforeseeable erroneous figures in the survey of the NRC concerning the glutamate consumption.

Based on published data (Nikkan Keizai Tsushinsha 1973), the production capacity of MSG in several countries is:

The Estimate on the Production Capacity (1973 Feb.)

Country	mt/year
U.S.A.	24,000
Japan	134,220
Korea	22,200
Taiwan	17,280
Thailand	14,160
France	12,000
Italy	10,800
Philippines	8,500
Indonesia	5,280
Malaysia	3,240
Peru	1,800
World Total Est.	262,000

Counted from the export and import (U.S. Tariff Comm. Report, 1971) approximate per capita consumption of MSG is:

USA	0.3 g/person/day
Japan	2.0

To the best of our knowledge, monoammonium glutamate is not widely used as a flavour enhancer for food. The consumption figure would never be over 1/100th that of MSG.

Missing Data

II. Missing Data

Results of critically designed animal studies including acute toxicity, subacute and chronic toxicity, reproductive, teratological, mutagenic and carcinogenic studies as well as biochemical and pharmacological behavior of a food chemical provide the crucial information in the evaluation of safety at a specified level of intake by man.

TRACOR-JITCO Scientific Literature Review of Glutamate misses a large number of data concerning animal experiments on toxicology, especially subacute and chronic toxicity studies.

Missing toxicological papers.

Acute toxicity

Published papers

1. Yanagisawa, K. et al., Nihon Seirigaku Zasshi (J. Physiol. Soc. Japan), 23, 383 (1968)

Unpublished papers

2. Ichimura, M. and Kirimura, J., Unpublished report (1968)

Subacute and chronic toxicity

Published papers

1. Hara, S., et al., J. Tokyo Med. Col., 20, 69 (1962)
2. Daniel, R.G. and Waisman, H.A., Growth, 32, 255 (1968)
3. Ebert, A.G., Toxicol. Appl. Pharmacol., 17, 274 (1970)
4. Wen, C-P, et al., Amer. J. Clin. Nutr., 26, 803 (1973)

Unpublished papers

5. Little, A.D., Unpublished report (C-58049) to International Minerals and Chemical Corporation (1953)

6. Little, A.D., Unpublished report (C-58047) to International Minerals and Chemical Corporation (1953)

Reproduction

Published papers

1. Semprini, M.E., et al., Quaderni della Nutrizione, 31, 85 (1971)

2. Prosky, L. and O'Dell, R.G., Experientia, 28, 260 (1972)

Unpublished papers

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4. Furuya, H., Unpublished report (1967)

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Teratology

Published papers

1. McColl, J.D. et al., Can. J. Physiol. Pharmacol., 43, 69 (1965)

2. US Food and Drug Administration "Report on monosodium glutamate for use in baby foods", Food Protection Committee, NAS/NRC (1970)

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Mutagenicity and carcinogenesity

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Missing papers in TRACOR-JITCO SLR concerning the effects on brain

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2. Lemkey-Johnston, N. and Reynolds, W.A., Anat. Rec., 172, 253 (1972)

3. Olney, J.W., Brain Res., 45, 309 (1972)

4. Matsuyama, S., et al., Nat. Inst. Am. Hlth. Quart., 13, 91 (1973)

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8. Lemkey-Johnston, et al., Anat. Res., 178, 401 (1974)

9. Nagasawa, H., et al., Acta Endocrinologia, 75, 249 (1974)

10. Reynolds, W., et al., Presented before The Anatomist's Meeting, Cleveland (1974)

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14. Oser, B.L., et al., Unpublished report to International Glutamate Technical Committee, (1973)

15. Reynolds, W.A. and Lemkey-Johnston,N., Unpublished report to International Glutamate Technical Committee, (1973)

Missing papers in TRACOR-JITCO SLR concerning the effects of massive ingection in human

Published papers

1. Smyth, C.J., et al., J. Med. Sci., 214, 281 (1947)

2. Levey, S., et al., J. Lab. Clin. Med., 34, 1238 (1949)

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2. Von Euler, H., et al., Z. Physiol. Chem., 254, 61 (1938)

3. Greenstein, J.P. and Carter, C.E., J. Nat. Cancer Inst., 7, 57 (1947)

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18. Adkins, J.S. et al., Proc. Soc. Exp. Biol. Med., 122, 519 (1966)

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9. Krnjevic, K., Nature, 228, 119 (1970)

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3. Bigwood, E.J. Present Problems in Nut. Research 88-99, 1952.

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Some pertinent papers appearing in the bibliography but not evaluated as part of feeding studies on Glutamate

Humans

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2. Zimmerman, F.T. and Burgemeister, B.B. ibid 81 649 (1959) (8286).

3. Jaeger-Lee, D.S. et al Dis Nerv. System 14 368 (1953) (3353).

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7. Waelsch, H. Am. J.Mental Defic. 52 305 (1948) (7790).

There are numerous feeding studies in laboratory and domestic animals which well illustrate toxic manifestations, often due to amino acid inbalance, and the lack of glutamate toxicity when glutamate is given at rates and routes common to its use by man.

Missing Data - Summary

P	¶	ℓ	
i	1,2,3,4	Last of each paragraph	Pertinent Data Omitted Implies only those specifications listed are in monograph. Incomplete, see Food Chemicals Codex or other official food compendia for total specifications.
ii	1	-	Missing Data - oral administration Glutamic Acid (5804) Rat P.O. > 30g/kg Rabbit P.O. > 23g/kg MSG (5804) Mouse P.O. 12961 " 16200 Rat P.O. 19900 " 10300 (DL Isomer)
P	¶	ℓ	
ii	iii	3	Comment "In 1957, they reported (4487) that single s.c. doses of MSG 4g/kg and up produced retinal lesions in neonatal mice within a few **hours of treatment."** Examination of this paper reveals that a 4g/kg dose gave no effect in 1/3 treated animals, 2/3 were rated as having "the slightest possible detectable lesion". To give marked retinal effects an 8g/kg dose was needed.
ii	iii	8	"...the smallest being 0.5g/kg i.p. for 16 days in adult rabbits (2770)." Statement implies 0.5g/kg gives characteristic retinal effect. Minimum dosage regimen of 2.2-4.2g/kg was required.

P	¶	ℓ	Comment
iv	ii	5	Of 24 compounds related structurally to MSG, glutamic, aspartic and cysteic acids were reported as neurotoxic." Reviewer fails to point out numerous compounds including methyl analogs of amino acids which were more potent in inducing neuronal effects.
v	2	4	"The results confirmed Olneys work". Suggests that the 0.5g dose mentioned on p iv was confirmed. It was not. Doses of 1g/kg causing neuronal effects were confirmed.
v	4	3	"in another study pyridoxine appeared to be involved, upsetting the balance of glutamate and GABA metabolism (0746)" Misleading description of glutamate effects in pyridoxine deficient rats needed here, see missing paper by Wen et al J. Nutr. 102 835 (1972).
x	2	3	"Recently, Van Harreveld and coworkers applied MSG to rat cerebral cortex by electrophoresis and produced spot lesions." None of Van Harrevelds work is applicable to human ingestion of glutamate and he has so stated.
xii	2	1	"No specific studies were found of the breakdown of salts of glutamic acid in the gut," well illustrates the fact that the reviewer does not comprehend that salts of glutamic acid are disassociated to ionized forms in the gut. Data on GA migration in gut have been published. See: Heame K.D. and Wiseman, G. J. Physiol (London) 133 39P (1956) (5233) J. Physiol (London) 135 442 (1957) (5235) J. Physiol (London) 138 41P (1957) (5236) J. Physiol (London) 176 33P (1965) (5237) J. Physiol (London) 140 148 (1958) (5238)

P	¶	ℓ	Comment
xiv	3	1	"Several studies have demonstrated a serum hypolipedemic effect on glutamate." Missing data on glutamate metabolism in humans that could be discussed here include: Stegink, L.D. et al Proc. Soc. Exp. Biol. Med 140 836 (1972) (8354) Stegink, L.D. Nutr. Rep. Int'l 3 93 (1971) (7014) Anon. Nutr. Rev. 28 158 (1970) (0268)
xiv	last		Data from other species missing includes: Shen, T.F. et al Poul Sci 52 676 (1973).

Missing Data - Text

P	¶	ℓ	Comment
23	"C"	1	The text fails to point out that automated methods using Amino Acid Analyzers are available and routinely used.
40	4	1	Data on Glutamic Acid content of the central nervous system incomplete. See text "Glutaminsaure" by W. Klingmueller.
46	3	1	No reports of glutamate tolerance curves in children have been found. These data are in Ref.7013, 7014. Also the group of interest is the infant - not child.
49-60			This section devoted entirely to acute or subacute parenteral administration to induce effects on the retina. No data or comparison with: routes of administration, dose, concentration, food use patterns.
73ff			No mention of: transient nature of effect as discussed in various Olney papers or of toxicology texts which point to permanency as a criterion for true toxic manifestations.

P	¶	ℓ	Comment
76	2		**No negative data in monkeys - see "Missing** papers in TRACOR-JITCO SLR concerning the effects on brain".
97	2	last	Missing data - see comments on summary
107	2	last	Re-dosing of vomiting animals has been described by Reynolds. Missing data - Newman et al. See comments on summary.
108	2	2	Old data - see comments on glutamate production above.
112	table 3		Fails to explain that Fig. 2 and Fig. 3 are actually in disagreement. Symptom sensitiveity = 1. just perceptive 2. moderately uncomfortable 3. severe - No person experienced "severe" burning, facial pressure and chest pressure. Fig. 2 reports maximum effects at 4g. Fig. 3 reports all effects at 4g below "just perceptible". At least 100% variation between results in Fig. 2 and Fig. 3 is evidenced.
127	2	last	Feeding data missing. Why not add statement describing how little glutamate enters the brain?
139	3	last	Missing Teratogenicity Data - See Summary

Editorial Statements - Summary

Throughout the summary and text, numerous editorial comments attacking glutamate are listed to the exclusion of remarks by those authors who have commented on glutamate safety.

P	¶	ℓ	Comment
iii	1	1	"Another author (1091) later commented that MSG was declared Generally Recognized As Safe (GRAS) the year after the Lucas and Newhouse report". This statement fails to reflect: 1. Statement made in a Letter to the Editor hence is not a part of the technical literature. 2. That the Lucas and Newhouse data were considered when the regulation was promulgated.
v	2	1	"To resolve these discrepancies" implies that the author had all the data and was in a position to pass judgment - a final word on this research. In fact, this author had no particular expertise, information or experience to resolve any "discrepancies".
vii	2	2	The remarks listed in the summary in no way respond to the criticisms of the work raised in the technical literature.
vii	2	last	One wonders why the reviewer does not comment on the non-physiologic nature of the emetic doses of glutamate given, and the de facto protective effects of emesis.
viii	1	4	"Many reports followed". Implies these were technical reports. They were in fact-largely confined to Letters to the Editor.
ix	3	1	Describes Olney editorial comments on glutamate in brain without discussion of any of the numerous other papers on glutamate as a neurohumor.

Editorial Statement-Text

P	¶	ℓ	Comment
30	3	2	Several workers have attempted determinations of the amounts of glutamic acid occuring naturally, but these are not easily made. Untrue - assays can certainly be done and there are numerous papers containing these data.

P	¶	ℓ	Comment
40	1		"only approximately accurate" Meaning?
40	2	1	"Maeda et al (4537) using a complicated microbiological quantitive analysis..." The method is no more complicated than other methods.
63	2	1	Refers to NAS/NRC report made on "limited and conflicting" data. Extensive data were, in fact, available. See comments summary section in "missing data".
81	1	3	The reviewer states that the authors refer to findings which were "entirely consistent" with Olney's (5483) and then lists data which - in fact - are not consistant with the data reported.
113	1	4	"Could produce undesirable effects in the amounts used in the preparation of widely consumed foods". Correct reporting of an editorial comment which is - in fact - untrue.
113	5	2	"questionable" (sic). Correct reporting - but an editorial criticism on of a bona fide toxicological complaint.
134	4	1	"The table reporting results of a second trial was not attached to the report". Untrue - all data were attached.
149	2	1	"But see pp 199-202" See discussion of NAS Data in "erroneous information" section.
182	2	1	"route preferred over stomach tube" - yes to give a toxic effect - not evaluate a food component.
213	1	1	"There are as many suggested usage levels for MSG as there are manufacturers and products". We know of publication of no such statement - the statement is clearly not true.
213	3	1	"Thus many experts have recommended that consumer exposures be restricted until safe levels have been defined by specific experimental evidence". Of course glutamate, is - in fact restricted in use and the specific experimental evidence has indeed been gathered and discussed.

P	¶	ℓ
213		1

Comment

"The Armed Forces now lists MSG as an optional ingredient in its U.S. recipes - As they always have.

General - While noting antiglutamate editorial comments the reviewer fails to list a single pro glutamate statement by a researcher. For the sake of such a list, completeness could have included: pro glutamate editiorial comments the latest of which is in Zbinden - Progress in Toxicology, Vol. 1 - Springer-Verlag, New York, 1973, P42